

U.S.S.N. 10/654,761
Filed: September 4, 2003
AMENDMENT AND
RESPONSE TO OFFICE ACTION

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for ~~extended and~~ controlled delivery of parathyroid hormone to a patient in need thereof comprising:
implanting a medical device into the patient, the medical device comprising a substrate, a plurality of reservoirs in the substrate, a release system contained in each of the reservoirs, wherein the release system comprises parathyroid hormone, and a plurality of discrete reservoir caps separating the release system from an environment outside of the reservoirs;
disintegrating one or more of the reservoir caps to expose the release system to the environment, wherein the disintegration occurs by electrothermal ablation; and
controllably-releasing a pharmaceutically effective amount of the parathyroid hormone from the reservoirs.
2. (Currently Amended) The method of claim 1, wherein the ~~step of controllably-releasing provides intermittent release of the~~ parathyroid hormone is released intermittently from the medical device.
3. (Original) The method of claim 1, wherein the parathyroid hormone is released daily in intermittent doses of between about 10 and 300 µg.
4. (Original) The method of claim 3, wherein the daily intermittent doses are released over a period of ten months or more.
5. (Original) The method of claim 1, wherein the parathyroid hormone is released in a pulsatile manner, each pulse having a duration of less than four hours.

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6. (Original) The method of claim 1, wherein the pharmaceutically effective amount of the parathyroid hormone, released over a first period of time, is effective to form bone tissue.
7. (Currently Amended) The method of claim 6, further comprising administering a pharmaceutically effective amount of a bone resorption inhibitor, released over a second period of time, to maintain bone tissue at a level present after the first period of time.
8. (Original) The method of claim 7, wherein the bone resorption inhibitor is selected from the group consisting of bisphosphonates, selective estrogen receptor modulators, calcitonins, vitamin D analogs, and calcium salts.
9. (Original) The method of claim 6, wherein the bone resorption inhibitor is administered orally.
10. (Currently Amended) The method of claim 6, wherein the bone resorption inhibitor is released from one or more reservoirs of in the medical device.
11. (Currently Amended) ~~The method of claim 1, wherein the patient is a female and the step of implantation of the medical device comprises~~ A method for controlled delivery of parathyroid hormone to a female patient in need thereof comprising:
 ~~inserting the a medical device into the vagina of the female patient, the medical device including a substrate, a plurality of discrete reservoirs in the substrate, and a release system contained in each of the reservoirs, wherein the release system comprises parathyroid hormone; and~~
 controllably releasing a pharmaceutically effective amount of the parathyroid hormone from the reservoirs.

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12. (Currently Amended) ~~A implantable~~ An implantable device for ~~the extended~~, controlled delivery of parathyroid hormone to a patient in need thereof comprising:

a substrate;

a plurality of reservoirs in the substrate;

a release system contained in each of the reservoirs, wherein the release system comprises parathyroid hormone; and

a plurality of discrete reservoir caps separating the release system from an environment outside of the reservoirs; and

means for disintegrating one or more of the reservoir caps by electrothermal ablation ~~a control means for selectively releasing a pharmaceutically effective amount of to release~~ the parathyroid hormone from ~~each of one or more of the reservoirs.~~

13. (Original) The device of claim 12, which is able to release a pharmaceutically effective amount of parathyroid hormone once daily over a period of at least six months.

14. (Original) The device of claim 12, further comprising at least one reservoir which contains a second release system comprising a drug other than parathyroid hormone.

15. (Original) The device of claim 14, wherein the drug is an anti-resorptive agent.

16. (Original) The device of claim 12, wherein each of the reservoirs contains between about 10 and 300 µg of parathyroid hormone for release.

17. (Original) The device of claim 12, wherein the plurality of reservoirs comprises 300 or more reservoirs, each containing a release system comprising parathyroid hormone.

18. (Original) The device of claim 12, wherein the release system comprises parathyroid hormone in combination with a pharmaceutically acceptable excipient.

19. (Original) The device of claim 12, wherein the release system comprises parathyroid hormone suspended in a non-aqueous vehicle.

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20. (Original) The device of claim 18, wherein the parathyroid hormone is dried or lyophilized with an excipient that promotes re-dissolution upon release.
21. (Original) The device of claim 18, wherein the excipient comprises polyethylene glycol having a molecular weight between about 100 and 10,000 Daltons.
- 22-23. (Cancelled).
24. (Currently Amended) The device of claim ~~23~~ 12, wherein the means for actively disintegrating comprises:
an electrical input lead and an electrical output lead electrically connected to at least one of the reservoir caps;
a power source; and
a control means for passing-controlling application of an electric current-or potential from the power source through said at least one of the reservoir caps, via the input and output leads, in an amount effective to electrothermally ablate said at least one reservoir cap.
- 25-26. (Cancelled).
27. (Original) The device of claim 12, further comprising a sensor.
28. (Currently Amended) ~~The device of claim 27, wherein the~~ An implantable device for controlled delivery of parathyroid hormone to a patient in need thereof comprising:
a substrate;
a plurality of reservoirs in the substrate;
a release system contained in the plurality of reservoirs, wherein the release system comprises parathyroid hormone;
a control means for selectively releasing a pharmaceutically effective amount of the parathyroid hormone from one or more of the reservoirs; and
a sensor which measures plasma calcium.

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29. (Canceled).

30. (Currently Amended) ~~The device of claim 29,~~ An implantable device for controlled delivery of parathyroid hormone to a patient in need thereof comprising:

a substrate;

a plurality of reservoirs in the substrate;

a release system contained in the plurality of reservoirs, wherein the release system comprises parathyroid hormone;

a control means for selectively releasing a pharmaceutically effective amount of the parathyroid hormone from one or more of the reservoirs, wherein the control means comprises multiple layers of release system having different compositions,

wherein a first two or more of the multiple layers comprise the parathyroid hormone dispersed throughout a solid matrix material comprising a water soluble polymer, and a second two or more of the multiple layers comprise the solid matrix material without parathyroid hormone, each of said first two or more layers being stacked alternately with said second two or more layers.

31. (Currently Amended) ~~The device of claim 29,~~ An implantable device for controlled delivery of parathyroid hormone to a patient in need thereof comprising:

a substrate;

a plurality of reservoirs in the substrate;

a release system contained in the plurality of reservoirs, wherein the release system comprises parathyroid hormone;

a control means for selectively releasing a pharmaceutically effective amount of the parathyroid hormone from one or more of the reservoirs, wherein the control means comprises multiple layers of release system having different compositions,

wherein said multiple layers comprises a first layer having a first concentration of parathyroid hormone therein, and a second layer having a second concentration of parathyroid hormone therein which is greater or less than the concentration in said first layer.

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32. (Original) The device of claim 12, capable of vaginal administration of the parathyroid hormone.
33. (Currently Amended) The device of claim ~~32~~ 30, wherein the substrate comprises a ring-shaped or rod-shaped body.
34. (Currently Amended) A- An implantable device for ~~the extended~~, controlled delivery of parathyroid hormone to a patient in need thereof comprising:
- a body;
 - a plurality of reservoirs in the body;
 - a release system contained in each of the reservoirs, wherein the release system comprises parathyroid hormone;
 - a electrically conductive reservoir cap covering each reservoir;
 - conducting leads to and from each reservoir cap; and
 - a power source and a controller for selectively delivering an electric current through the reservoir cap effective to rupture the reservoir cap and release a pharmaceutically effective amount of the parathyroid hormone from the reservoir.
35. (Original) The device of claim 34, wherein the release system comprises multiple layers of release system having different compositions.
36. (New) The device of claim 34, wherein the release system comprises parathyroid hormone is in a dried or lyophilized form and a polyethylene glycol.
37. (New) The device of claim 31, wherein the substrate comprises a ring-shaped or rod-shaped body.